UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte WENDY MAURY, JACK STAPLETON, RICHARD ROLLER, MARK STINSKI, PAUL B. MCCRAY, and BRIAN TACK

Appeal 2007-1621
Application 10/721,839
Technology Center 1600

Decided: July 24, 2007

Before TONI R. SCHEINER, DONALD E. ADAMS, and ERIC GRIMES, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to reducing the infectivity of a virus by administering a chimeric theta defensin peptide. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

BACKGROUND

"Antimicrobial peptides have been isolated from plants, insects, fish, amphibia, birds, and mammals. Although previously considered an

evolutionarily ancient system of immune protection with little relevance beyond minimal primary protection, recent developments have found that mammalian cells express these peptide antibiotics during inflammatory events such as wound repair, contact dermatitis and psoriasis" (Specification 2, citations omitted).

Thus, antimicrobial peptides "are apparently a primary component of innate host protection against microbial pathogenesis" (*id.* at 2). In the prior art, for example, "[a] series of synthetically derived theta defensins from rhesus macaques (RTD 1-3) have been shown to exhibit bactericidal activity" (*id.* at 9).

The Specification discloses that when theta defensin peptides were tested for antiviral activity, both the oxidized (linear) and oxidized circular forms of the peptides "effectively inhibited HIV replication in HeLa cells" (*id.* at 10). The Specification discloses methods for inhibiting viral growth and proliferation by administering any of a number of antiviral peptides ranging from 13 to 35 amino acids in length, including chimeric human/rhesus monkey theta defensins having SEQ ID NOS: 31 and 32 (*id.* at 3).

DISCUSSION

1. CLAIMS

Claims 1, 9, 18-24, 27, 28, 34-38, and 40 are on appeal. Claims 10-15, 25, 26, and 29-33 are also pending but have been withdrawn from consideration by the Examiner.

The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). We will focus on claim 1, the broadest claim on appeal, which reads as follows:

> 1. A method for reducing the infectivity of an enveloped virus comprising contacting said virus with a first anti-viral peptide, said peptide comprising a chimeric theta defensin peptide selected from the group consisting of SEQ ID NO:31 and SEQ ID NO:32

2. PRIOR ART

The Examiner relies on the following reference:

Lehrer	WO 02/085401 A1	Oct. 31, 2002

3. OBVIOUSNESS

Claims 1, 9, 18-24, 27, 28, 34-38, and 40 stand rejected under 35 U.S.C. § 103 as obvious in view of Lehrer (Answer 3).

The Examiner cites Lehrer as teaching "the making and use of theta defensins comprising an amino acid sequence formed from any combination of two nonapeptides selected from those disclosed as SEQ ID NOs: 19-64 in the reference. See, e.g., claim 6" (*id.* at 4). The Examiner states that Lehrer "teaches that these defensins may be administered to a subject with a viral infection, [or] facing exposure to viral infection, including infection by HIV" (*id.*).

The Examiner concedes that Lehrer "does not verbatim teach the use of the peptides of SEQ ID NOs: 31 and 32 of the present application" (*id.*). Despite this, the Examiner urges that Lehrer suggests administering those peptides to combat viral infection because Lehrer "teaches the combination

of any of the specifically disclosed nonapeptides for the formation of a theta defensin[] for use in the indicated methods" (*id.*).

The Examiner reasons that although Lehrer "does not lay out each of the indicated defensin peptides individually, by setting forth the nonapeptides from which they are made, the reference nonetheless sets forth a specific set of defensin peptides that may be immediately envisaged by those of ordinary skill in the art" (*id.*). The Examiner concludes that Lehrer therefore teaches that "each of the peptides formed by each combination of two of the nonapeptides disclosed on pages 7-8 of the reference" would be useful in treating viral infections, as recited in claim 1 (*id.*).

To show that a combination of Lehrer's nonapeptides results in the peptides of claim 1, the Examiner initially notes that, because Appellants' claimed peptides are circular, their amino acid sequences can be validly represented as starting from position 4, as follows (*id.* at 3):

	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 1 2 3
SEQ ID NO: 31	R–C–L–C–R–R–G–V–C–R–C–I–C–G–R–G–I–C

	4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 1 2 3
SEQ ID NO: 32	R–C–I–C–T–R–G–F–C–R–C–I –C–G –R–G–I–C

The Examiner states that when nonapeptides 27 and 34 of Lehrer are linked, the resulting peptide sequence is identical to that of realigned SEQ ID NO: 31 (*id.* at 5), and that the peptide made by linking nonapeptides 18 and 34 of Lehrer demonstrates that SEQ ID NO: 32 "is also among the defensins contemplated by the Lehrer reference" (*id.*). The Examiner concludes that "[t]hose of ordinary skill in the art would have had a reasonable expectation of success in the disclosed use of such peptides based

on the suggestion in the reference that each of the defensin peptides derived from the disclosed nonapeptides would be useful in the claimed methods" (*id.*).

We agree with the Examiner that, in view of Lehrer's teachings, one of ordinary skill in the art would have considered it obvious to use peptides with the sequences set forth in SEQ ID NOS: 31 and 32 to reduce the infectivity of an enveloped virus.

Specifically, Lehrer discloses "using retrocyclin (*e.g.* RC-101) or a retrocyclin analog to prevent or treat infection, for example by an enveloped virus, including enveloped retroviruses, more specifically by HIV-1, HIV-2 and related retroviruses that cause Acquired Immunodeficiency Syndrome (AIDS)" (Lehrer 6). Lehrer states that "[f]or use in the subject methods, a naturally occurring or synthetic retrocyclin may be used" (*id.*).

Lehrer states that "[r]etrocyclins are octadecapeptides that contain two linked nonapeptides that may be identical or different" (*id.* at 7). Lehrer discloses that the nonapeptides making up retrocyclins have a consensus amino acid sequence (*id.*), and provides a list of the 46 nonapeptides derived from the consensus sequence (*id.* at 7-8). Linking nonapeptide 27 with nonapeptide 1 yields a sequence identical to SEQ ID NO: 31, when allowance is made for the circular nature of the peptides.[1] Linking

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[1] The Examiner asserts that the combination of nonapeptides 27 and 34 results in SEQ ID NO: 31 (Answer 5). However, due to an apparent typographical error, nonapeptide 34 is incorrectly depicted as having the same sequence as nonapeptide 1, RCICGRGIC (Lehrer 6). Nonapeptide 34 apparently has the sequence RCLCVRGFC, as evidenced by the modifications to the consensus sequence being listed s "L3, V5, F8" (*id.*)

nonapeptide 18 with nonapeptide 1 results in a sequence identical to SEQ ID NO: 32, when the same circular peptide allowance is made.[2]

Thus, one of ordinary skill would have recognized that, by following Lehrer's explicit directions for making retrocyclins, one would obtain a set of retrocyclins that included peptides having SEQ ID NOS: 31 and 32. Because Lehrer teaches "using retrocyclin . . . or a retrocyclin analog to prevent or treat infection, for example by an enveloped virus" (Lehrer 6), we agree with the Examiner that one of ordinary skill would have considered it obvious to contact peptides having SEQ ID NOS: 31 or 32 with an enveloped virus to reduce the virus' infectivity.

Appellants argue that, because "findings of fact by the Board of Patent Appeals and Interferences must be supported by 'substantial evidence' within the record . . . , it necessarily follows that an Examiner's position on Appeal must be supported by 'substantial evidence' within the record in order to be upheld" by the Board (Br. 3,[3] citing *In re Gartside*, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000)).

We do not agree. *Gartside* only applies to review of the decisions of this board by the Court of Appeals for the Federal Circuit. *See Gartside*, 203 F.3d at 1315, 53 USPQ2d at 1775 ("'[S]ubstantial evidence' review

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Thus, the actual combination of peptides resulting in SEQ ID NO: 31 is nonapeptides 27 and 1.

[2] Lehrer's nonapeptide 18 has the sequence RCICTRGFC (Lehrer 8). The Examiner's comparison of "Lehrer 18 and 34" to SEQ ID NO: 32 incorrectly shows that Lehrer's nonapeptide 18 has an L at the third position (Answer 5; *see* position "6" in the comparison of Lehrer 18 and 34 to SEQ ID NO: 32).

[3] Appeal Brief filed October 10, 2006.

applies when the reviewing court must confine its review of agency factfinding to the record produced by the agency proceeding."). It does not apply to review of an Examiner's rejection by this board. "[T]he conclusion of obviousness *vel non* is based on the preponderance of evidence and argument in the record." *Id.* at 1446, 24 USPQ2d at 1445. *See also In re Kahn,* 441 F.3d 977, 989, 78 USPQ2d 1329, 1338 ("[T]he Board need only establish motivation to combine by a preponderance of the evidence to make its *prima facie* case."). In practical effect, this review is *less* deferential to the Examiner than the standard urged by Appellants: any decision that is supported by a preponderance of the evidence is also supported by substantial evidence.

Appellants argue that, because Lehrer discloses that retrocyclins are a combination of two nonapeptides selected from a list of 46 nonapeptides (SEQ ID NOS: 19-64), Lehrer discloses a genus having 46 X 46, or 2116 members (Br. 4). Appellants argue that the Examiner "has found, using appellants' claims as a searching point, that SEQ ID NOS:31 and 32 can be identified as members of the 2000+ peptide genus described by Lehrer, and appellants do not disagree. However, this is far short of what is needed to find obviousness in this situation" (*id.*). Appellants argue that "the question boils down to whether one of ordinary skill in the relevant art would have been motivated to select the claimed species from the prior art genus" (*id.* at 7; *see also* Reply Br. 5).

Appellants argue that, in determining whether a prior art genus renders a species claim obvious, the size of the genus "is a relevant factor, with the larger the genus and the smaller the selection arguing in favor of

patentability" (Reply Br. 6). Appellants argue that in the instant case "there is a large genus, and more importantly, no discussion of why the claimed species would have been selected" (Br. 8), and therefore the Examiner has not shown sufficient motivation to select the claimed peptides from among those disclosed in Lehrer (*id.* at 9).

We do not agree that Lehrer's disclosure would have failed to provide sufficient reason to make the peptides of SEQ ID NOs 31 and 32 and use them to reduce the infectivity of an enveloped virus. Lehrer explicitly states that retrocyclins are useful for inhibiting enveloped viruses, including HIV (Lehrer 6), and that such retrocyclins are made by linking any two of 46 explicitly disclosed peptides (*id.* at 7-8). It is undisputed that selecting the appropriate peptides from Lehrer's list of 46 suitable variants results in SEQ ID NOS: 31 and 32. The reason one of ordinary skill would have selected the building blocks resulting in the peptides of claim 1 is that Lehrer disclosed that they were among the peptides suitable for preparing antiviral peptides.

Moreover, we do not agree that the appealed obviousness rejection fails to meet the standard set MPEP § 2144.08 and the cases cited therein. For example, in *In re Jones*, 958 F.2d 347, 350 21 USPQ2d 1941, 1943 (Fed. Cir. 1992), the court held a species claim to be unobvious over a genus that was "potentially infinite," the claimed compound also having significant structural differences compared to the primary reference. Similarly, in *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994), the prior art disclosed a generic formula encompassing "more than 100 million different diphenols[,]" and the reference's fifteen preferred compounds did

not disclose, or even suggest the claimed compound. *See also, In re Bell*, 991 F.2d 781, 784, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993) (species claim held unobvious over genus encompassing "more than 10^{36} different nucleotide sequences"); *In re Deuel* 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995) (species claim held unobvious over genus encompassing "an enormous number of DNA sequences").

Rather than requiring the artisan of ordinary skill to select from a genus having many millions of possible choices, Lehrer only requires the practitioner to choose a first nonapeptide from among 46 possibilities, and a second nonapeptide from the same list of 46 members. Thus, the situation faced by the artisan of ordinary skill practicing Lehrer's disclosure is not analogous to that in *Jones*, *Baird*, *Bell*, and *Deuel*, in which species claims were held unobvious over huge genera. Rather, because preparing antiviral retrocyclins according to Lehrer's disclosure requires selecting only two nonapeptides from a list of 46, in our view, the instant situation is more similar to that of *Merck & Co. Inc. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807, 10 USPQ2d 1843, 1846 (Fed. Cir. 1989).

In *Merck*, the court held a species claim obvious over a reference disclosing over 1200 possible combinations of two ingredient types useful in diuretic compositions, where the claimed combination was one of those disclosed. *Id.* at 806-807, 10 USPQ2d at 1845-1846. Neither of the claimed ingredients was listed by the reference as being preferred. *Id.* The court nonetheless held the claims to be obvious in view of the reference's explicit teaching that any one of the claimed compositions would produce a diuretic composition having desirable properties. *Id.* at 807, 10 USPQ2d at 1845-

1846. Like the situation in *Merck*, the artisan of ordinary skill need only make two choices from a list explicitly set forth in the Lehrer reference. In our view, the Examiner properly concluded that one of ordinary skill would have considered claim 1 obvious over Lehrer.

Appellants argue that inhibition of HIV is unpredictable, and that "[w]here unpredictability undercuts any likelihood of success, as is the case here, there *is* no *prima facie* [case of obviousness]" (Br. 10). Appellants urge that the unpredictability in the field is demonstrated by Lehrer's disclosure that most of the mono-tyrosine substituted retrocyclin variants were either inactive or only modestly active against HIV-1 strain IIIB, and that variants RC-106, RC-107, and RC-108 "were not functional against the JR-CSF strain, either" (Reply Br. 7).

We do not find these arguments persuasive. While Lehrer discloses that certain tyrosine-substituted peptides were less effective in inhibiting HIV-1 infection, none of Lehrer's 46 variations on the retrocyclin consensus sequence has a tyrosine (Y) substitution (*see id.* at 7-8). Thus, no member of Lehrer's genus has the amino acid substitution urged by Appellants to undermine the predictability of Lehrer's disclosure.

Moreover, it is well settled that "[o]bviousness does not require absolute predictability of success. . . . [A]ll that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). In the instant case, claim 1 only requires the peptide to "reduc[e] the infectivity" of any enveloped virus. Claim 1 therefore encompasses even very small levels of infectivity reduction.

Lehrer discloses that "[r]etrocyclin was uniformly protective against both strains of HIV-1 in all of the experiments," and that certain variants "showed considerable ability to protect cells from infection by the JR-CSF strain" (Lehrer 23). Given Lehrer's explicit disclosure that retrocyclin and certain variants protected cells from HIV infection, we agree with the Examiner that one of ordinary skill would have had a reasonable expectation that selecting from among Lehrer's list of 46 suitable variants would have produced a retrocyclin capable of reducing the infectivity of an enveloped virus, as recited in claim 1.

To summarize, we agree with the Examiner that one of ordinary skill following Lehrer's teachings would have considered it obvious to use the claimed peptides to reduce the infectivity of an enveloped virus. We therefore affirm the Examiner's obviousness rejection of claim 1 over Lehrer. Because they were not argued separately, claims 9, 18-24, 27, 28, 34-38, and 40 fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

AFFIRMED

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